DECLARATION UNDER RULE 132

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First Inventor	HOSTETTER
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Examiner	Devi, Sarvamangala J.N.
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Commissioner for Patents
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S I R:

I, Dr. Margaret K. Hostetter, M.D., declare and say as follows:

1. I am the first named inventor of the above identified application. I am a Professor and Chair of the Department of Pediatrics and Physician-In-Chief for Yale New Haven Children's Hospital of the Yale University School of Medicine. I have also been an inventor or co-inventor on numerous patents and articles in the field of the present invention. I am thus well familiar with the subject matter of the claims of the present application.

2. The present invention is directed to the recent discovery of the propeptide sequence of the Int1p protein of *Candida albicans* and the role in plays in the activation of T lymphocytes in host cells. As is set forth in the specification of the above application, it was discovered that the propeptide is a superantigen-like moiety which is cleaved from Int1p which triggers activation of T lymphocytes.

3. In the present application, we have discovered that discovered that antibodies to the propeptide region, i.e., amino acid residues 1-263 of the Int1p

protein, have the ability to prevent release of the superantigen and thus inhibit the activation of T lymphocytes caused by *C. albicans*. In particular, antibodies to the propeptide region in accordance with the invention block the cleavage site and inhibit cleavage of the propeptide, and thus are capable of inhibiting the activation of T lymphocytes in a manner not previously possible using prior antibodies to Int1p.

4. In my prior patents, including U.S. Patent No. 5,886,151 and 6,774,219 (issuing from cited U.S. Pat. App. Ser. No. 09/978,343), antibodies were disclosed which were capable of recognizing the Int1p region, and we reported that such antibodies were able to block adhesion of *C. albicans* to host cells. However, the fact that the prior antibodies could block adhesion has nothing to do with the ability to prevent cleavage of the propeptide and inhibit T lymphocyte activation. Accordingly, because the prior antibodies were **not** directed to the propeptide region they did **not** exhibit the properties of the antibodies of the present invention, namely preventing the cleavage of the propeptide and inhibiting the activation of T lymphocytes. Indeed, unlike the present antibodies to the propeptide region, the prior antibodies associated with our prior work on Int1p did **not** show an ability to inhibit T lymphocyte activation. My prior patents thus do not disclose or suggest antibodies to the propeptide region which unexpectedly have the ability to prevent the cleavage of the propeptide and inhibit activation of T lymphocytes.

5. Further, our laboratory has performed additional tests of the ability of the antibodies in accordance with the present invention to bind to the propeptide region so as to prevent the formation of cleaved superantigen and prevent T lymphocyte activity. In these tests, two different antibodies capable of binding to

the propeptide, identified as "MAb 163.5" and "MAb 253", were introduced at various dosages, and the inhibition of T lymphocyte was monitored in each case. The table that follows below represents the percentage of inhibition of T lymphocyte activation:

Antibody	Dose Concentration (µg/ml)	Inhibition of T lymphocyte activation (% inhibition)
MAb 163.5	80	75
MAb 163.5	70	75
MAb 163.5	50	75
MAb 163.5	25	50

Antibody	Dose Concentration (µg/ml)	Inhibition of T lymphocyte activation (% inhibition)
MAb 253	70	85
MAb 253	50	85
MAb 253	25	50

6. As shown above, the present antibodies to the propeptide region provide unexpected and enhanced benefits in terms of inhibition of T lymphocyte activation in a manner not disclosed or previously suggested by our prior work. These studies show that relatively low amounts of antibodies can be used to achieve relatively high levels of inhibition of T lymphocyte activation, and such an unexpected benefit will be useful in the prevention and treatment of the diseases associated with *C. albicans*.

I further declare that all statements made herein are true and correct to the best of my knowledge and that all statements made on information and belief are believed to be true to the best of my knowledge; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated _____

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Margaret K. Hostetter

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